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LEAGUE OF NATIONS.

Health Organisation.

A MEMORANDUM

ON THE

EPIDEMIOLOGY OF CHOLERA

BY

Major A. J. H. RUSSELL, M.A., M.D., D.P.H., I.M.S.,
Director of Public Health, Madras Presidency, India.

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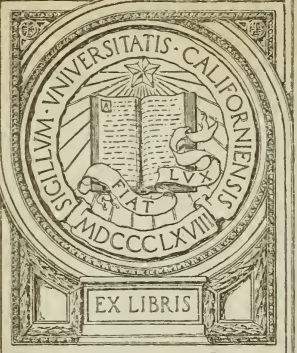

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CONTENTS.

	Page
Historical Introduction	5
Endemic Centres	7
Cholera-carriers	12
Pandemics	14
Routes of Spread to the West	16
Pilgrimages, Fairs and Religious Festivals	22
Routes of Spread in the Far East	23
Climatic Conditions	25
Seasonal Prevalence	35
Periodicity of Cholera Epidemics	36
Food Supply and the Vitality of the Population	40
Conclusion	40
Summary	41
Bibliography	43

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THE EPIDEMIOLOGY OF CHOLERA.

HISTORICAL INTRODUCTION.

The disease known as cholera is described by Hindus, Chinese, Arabs, Greeks, Romans and other ancient writers of the pre-Christian era. HIPPOCRATES, in his *De Morbus Popularibus*, lib. 5, enters into details respecting the history and symptoms of the disease. ARETŒUS, lib. 2, chap. 5, gives an admirable account of the disease; CELSUS, lib. 4, delineates its most striking features; whilst it is also mentioned by CŒLIUS AURELIANUS and other Roman writers. In ELLIOT'S *History of India*, cholera is mentioned as probably occurring there in 1325, and in Europe from the 16th century. Cholera appeared in the year 1503 in one of the first European campaigns in India, and the disease can be distinctly traced from the 15th century onwards. The first undoubted epidemic noted by Europeans took place in 1543 in Goa, Gaspar CORREA describing an outbreak there in that year. The disease was given the name of "moryxy", and in the earliest European work on Indian medicine, which was published by Garcia D'ORTA in 1563, the symptoms are fully described. In CURTIS' *Diseases of India*, it is said that cholera appears to have first shown itself in India, at Madras, in 1774, whilst in 1780 it destroyed 20,000 persons at the Hurdwan festival; but Dr. Kanta SIRCAR [1] * thinks it "reasonable to suppose that the disease must have existed before the arrival of the Portuguese in 1498. In the 17th century there are abundant traces of cholera, and its spread was fostered by the trade that sprang up between the islands of Java, Sumatra, etc., and India."

Zacutus BONTIUS and others describe outbreaks about 1532, widely diffused in Java, India, Arabia and Morocco. Apparently a quiescent period occurred in the early 18th century, followed by a great outburst in 1756 which lasted about thirty years. This was succeeded by another quiescent period until 1817, when cholera broke out at Jessore, about 60 miles from Calcutta, and ultimately spread over the whole country. The Jessore outbreak seriously affected Lord HASTINGS' army formed to fight the Pindharis, and was therefore the first widespread epidemic to receive detailed attention in the current literature. It is apparently due to this fact that the mistake has been repeatedly made of referring to the Jessore epidemic as the first appearance of cholera in India. It is certain, however, that cholera existed in India for centuries before HASTINGS' recorded experience, and [2] "the

[1] These numbers refer to those given in the Bibliography on page 43.

first thing to be clearly understood is that this is no new enemy of mankind which arose in the district of Jessore in 1817, as has been generally supposed. The description given in these early records is unmistakable, while the fact that such cases occurred not only in individual instances but also in severe epidemics leaves no doubt that the cholera of India to-day is exactly the same as it was at least four hundred years ago, and as it probably ever has been."

Macpherson (3) writes:

> "Since 1817, there has been no true period of quiescence, nor at the present day is cholera unknown in any one of the districts in which we have the earliest accounts of it. Since 1821, cholera has prevailed nearly every year in some part of Persia or the Persian Gulf, very constantly in Arabia and occasionally on the shores of the Red Sea."
>
> "In Madras cholera epidemics have been described since 1757, and Dr. Paisley of Madras gives details of more than one epidemic, estimating that over 60,000 people between Cheryan (on the delta of the Cauvery) and Pondicherry were carried off by it. In 1782 and 1783, another two epidemics occurred in Madras. The disease was met with in Vellore and Arcot in 1787, and on the Chilka Lake in 1790. The maximum intensity occurred from 1775-1785 in the period 1756-1797, and then apparently a twenty-years period of quiescence was experienced. An epidemic occurred in Trincomalee in 1804, in Jalna in 1814, and then Jessore in 1817."
>
> "The portion of India known as the Madras Presidency, and in a general way representing the eastern coast of the Peninsula, was a constant seat of the disease from the middle of the 18th century, and for a period of thirty years its epidemic ravages in that part of India were frequent. The town of Madras often suffers from epidemics, and the high plateau of Mysore also occasionally suffers. The ceded districts appear of late to have been its favourite seat."
>
> "Cholera in its worst form was fairly introduced into Bengal in 1781, but did not fructify there as it has done since 1817, when apparently both Europeans and natives had almost forgotten the previous epidemic."

Macpherson adds that "there can be no doubt that the endemic of Travancore was the epidemic of other parts. We have thus traced an endemic cholera prevailing at times with epidemic violence in the west and southern parts of the Indian peninsula from the earliest European times to 1818, and it is not till that period that there is the slightest occasion to allude to Bengal or the distant delta of the Ganges".

The author scoffs at the conclusions of the Constantinople Conference, which declared that "cholera seems to be an original product of the valley of the Ganges, that the disease is the result of new conditions produced in India about 1817, and that cholera, being only of late years in a state of permanence, must be due to some new and special conditions of those localities".

The author concludes: "(*a*) that cholera of varying intensity has always prevailed in India; (*b*) that the disease has existed as an endemic in the East as long back as we have any certain European accounts; (*c*) that the great characteristic of the disease is its epidemic diffusion — early notices of the disease represent it as endemic with a tendency to become epidemic; and (*d*) that although it may break out and there may be even partial epidemics at almost every season, each district in India has its season when cholera prevails most frequently."

FAYRER (4) says that nothing exists in the records to prove that the origin of cholera is to be traced to India alone.

NOTHNAGEL (5), on the other hand, asserts that "cholera appears to have originated in India, and the epidemic of 1817 first drew attention of European physicians to Asiatic cholera. The precise home of the disease where all epidemics originate is Hindustan, and especially the lowlands of Bengal near the mouths of the rivers Ganges and Brahmaputra".

In reviewing the historical records, one is forced to the conclusion that cholera has existed in India for many centuries in much the same form as it exists at present. It is fairly certain also that the disease was known practically all over the East, as very early references are made to its presence in Persia, Arabia and Java. With regard to MACPHERSON's arguments that Bengal is not the primary endemic seat of cholera, it may be remarked that the west coast of India, *e. g.*, Goa, and the south-east coast of the Indian peninsula were visited at a much earlier date by Europeans than the valleys of the Ganges and the Brahmaputra, and it is therefore only to be expected that notices of cholera epidemics in Goa and Madras would be the first to appear in European records. It is difficult to believe, moreover, that cholera did not exist in Bengal prior to 1787 or 1817, when so many definite references are made to its earlier existence in epidemic form in other parts of India. One is bound to conclude that MACPHERSON did not prove his case, but, at the same time, NOTHNAGEL's dogmatic opinion is probably equally in error.

ENDEMIC CENTRES.

Controversy regarding the so-called endemic centres of cholera has raged since the attention of Europe was drawn to the disease in 1817.

FARR (6) makes the statement that, "in the meantime, it is difficult, looking at the chain of evidence, to refuse the conviction that Asiatic cholera came from Asia". "To render the generation of great epidemics of cholera rare, nay improbable, India has only to carry out the measures which have proved efficacious in England". At the international Cholera Conference at Constantinople, "a large share of the measures proposed are directed towards India and the cholera routes between India and Europe". "The cities, the pilgrims and the religious festivals

must be brought under regulation to secure the nations of the world from evils against which they have a right to demand protection."

Macpherson (3) says: "Too much attention has been attached to the Gangetic valley as a generator of cholera, whereas, from the earliest date, cholera has existed as an endemic in other parts of India quite independently of Lower Bengal, and it so happens that historically Bengal is the part of India in which no account of the very early prevalence of the disease has been discovered." His conclusion that cholera of varying intensity has always prevailed in India is corroborated by Bellew (2).

Fayrer writes that places from which cholera is never absent, according to Corré (7), comprise India, Indo-China and a part of the Malay Archipelago. In India, it is not confined to Lower Bengal and the delta of the Ganges, but is endemic and widely distributed in the deltas of the Brahmaputra and Mahanuddy, the interfluvial tracts of Behar, the deltas of the Irrawaddy, Godaveri, Kistna, and Cauvery, the Konkan and Malabar coasts, the southern half of the North-West Province and Oudh, Gurgaon, Delhi and Karnal districts between the Jumma, Sutlej, etc. The following authorities are quoted by the same author. Hunter (8) shows cholera to be endemic in Egypt and asserts that in "parts of Russia there can be little doubt that it is so". Hutchinson (9) says: "There is no such thing as Asiatic cholera if we mean by Asiatic that the disease is prevalent in India alone or any given part of the Eastern continent". Cunningham (10) writes: "Even in the endemic districts the difference between an epidemic and a non-epidemic year is very striking". "Great variations in intensity occur everywhere in India". Dr. Bryden believes that "cholera has a perennial abode in certain areas in India and in other districts is renewed by invasion from these areas."

Fayrer's conclusions are: "(*a*) Cholera is always present not only in certain parts of India but elsewhere; (*b*) cholera does not attack all the places within an epidemic area; and (*c*) meteorological changes produce sudden alterations in the activity and intensity of an outbreak".

Willoughby (11) states that "in Bengal cholera is never absent, the microbes existing and perpetuating themselves in the soil; in other parts of India they remain dormant in the soil, ready to break forth into activity at various intervals depending on seasonal conditions or aggregations of human beings".

Tholozan, J. D. (12), in discussing the places of origin or emergence of great epidemics of cholera, and particularly that of 1846-49, writes: "No serious examination of this epidemiological problem has been made to this day." He quotes Dr. Arnott's paper to the Physico-Medical Society of Bombay, which states that, at the end of the summer of 1844, the countries north of Hindukush were devastated by cholera, Boghara and Balkh losing about 25,000 inhabitants; Samarkand and

Kunduz suffered as much. Gradually the infection spread south-east through Afghanistan and, in early November, reached Peshawar, whence it spread all over the Punjab and as far as Karachi. In September 1845, cholera reached Kandahar and Ferrah; in October, Herat became infected, and by 1846 the disease was carried to Asterabad, Teheran, Baku and Astrakhan. The author says there can be no question of a province of India being the source, as the epidemic was traced from west to east, contrary to the direction of the epidemics, which start in India from the endemic zone and spread south-east and north-west. This epidemic shows the transport of infection from a central point in Asia to the confines of "l'aire épidémique ". The more he studies the question the more he is convinced that "les points d'emergence " of cholera epidemics ought to be considered as their focus of origin.

> "The idea that the different pandemics of cholera all start in India cannot be maintained. Two examples from Europe alone can be taken to explode finally the theories which have only the Orient in view as a danger of contamination. The epidemic of 1852 came from the borders of Poland and Germany, and it had there its point of departure. The epidemic of 1869-73 repeated the same facts in the Ukraine. Some maintain that these epidemics rose from still previous epidemics starting in India.
>
> "What makes the invading epidemic or the pandemic is the revivifying of the cholera germ or virus. This revivification occurs in India and is responsible for the perpetuation of annual endemics and epidemics which recur every three, four or five years. This is the primordial fact which governs the whole history of cholera, and it is on this that we should carry out research. What difference of morphology, virulence or power of reproduction is there between the germs of epidemics which remain confined to one place and those of the epidemics which spread all over the world, even though they do not start in India ? "

Ernest Hart ([13]) bluntly calls the region of the Lower Ganges "the home of cholera ", and adds that, from the conditions there of air, water and soil, and the habits of the people, there is nothing strange in cholera becoming endemic in this area. He also states that "Mecca is the centre of infection and the progress of cholera in Egypt and Europe will never be checked until it is cleaned up. " "This infection from Mecca is not the infection which is brought from India, but a fresh generation born at Mecca, which would never have come into existence at all but for the uncleanliness of the place. "

Colonel King ([14]) apparently also believes that Bengal is *the* endemic centre, for he writes : "It has nevertheless always seemed to me theoretically probable that invasion of Madras Presidency from the endemic area of Bengal and exacerbation of the virulence of microbes left from the last invasion in the soil and water may occur under certain meteorological and subsoil water conditions, so that invasion and endemic waves overlap. "

The report of the United States of America Commission ([15]) concludes that, "by general consent, among various authorities on cholera, it appears that there is a certain area bounded by more or less indefinite limits where cholera is always endemic in India, *i.e.*, the Presidency of Bengal."

Herbert ([16]) believes and has reasons for saying that "cholera is very generally endemic in some degree throughout the greater part of India". In dealing with provinces, he classed the Punjab as non-endemic. "The bulk and the extent of the travelling west from the delta of the Ganges to other areas have been exaggerated."

Proust ([17]) says: "Without doubt, cholera exists constantly in an endemic state in certain parts of India, notably Calcutta and Bombay, and the disease does not affect the natives of a place as much as the non-acclimatised stranger. In endemic foci the natives become immune, so to speak undergoing a cholera vaccination, and strangers coming from the interior get the disease and propagate it, especially at the times of the seasonal recrudescences."

Bruce Low ([18]), in discussing the cholera outbreak of 1902, states that "it is not certain what was the source of the cholera which broke out among the Mecca pilgrims and spread to Egypt, Palestine and Syria, but it is said to have been brought from Java in a pilgrim ship." He doubts "the suggestion that it was brought from India, though it may have come thence by land in caravans from Mesopotamia. Even the Egyptian epidemic cannot be definitely said to have been proved to be due to pilgrims from Mecca."

Dr. Slatogoroff ([19]) states that "cholera was most prevalent in the neighbourhood of the Shat-el-Arab, where it was a permanent endemic under conditions similar to those existing on the Ganges."

Bruce Low, in 1908, mentions ([20]) that cholera was very severe in Russia in 1907 up to February 1908, and spread from Russia to Asiatic Turkey and to Persia. Regarding Turkey, "two Russian vessels with pilgrims on board arrived at Yanbo in December with cholera on board. From Yanbo, cholera was carried overland to Medina and Mecca. These facts go to prove that the infection of the Hedjaz by cholera at the end of 1907 was not brought from India, but from Russia, where the disease had been epidemic in the autumn and winter months."

It is stated ([88]) that Russia acted in 1910 as the chief diffusing centre for the rest of Europe, and, from the Russian provinces south of the Caucasus, cholera was carried into Turkish territory to Van, Erzerum and Trebizond, and finally to Constantinople.

Simpson ([21]) says that certain localities in Russia near the Caspian Sea have been so often attacked that it is a question whether the disease has established an endemic centre there as it has done in the Far East, in Java, Indo-China and the Philippines.

The source of the nine invasions into Europe has generally been traced to India, Mecca playing the part in most instances as a great disseminating centre.

T. Kabeshima (22) insists that "cholera is not endemic in Japan. It is always imported and usually appears first among fishermen of the coast". The same opinion was expressed by one of the official Japanese delegates at the Far Eastern Association of Tropical Medicine (89) held in Singapore in 1923.

Hoops (23) is convinced that cholera was not imported into Kedah in 1916, though textbooks give it as a truism that cholera is an imported disease.

None of the outbreaks in Kedah have been traced to an imported cause. From experiments carried out with cultures of the *vibrio choleræ* in different water samples, Stanton formed the hypothesis that in certain areas in Kedah there was a natural reservoir of virus, the renewed activity of which was derived from some special combination of circumstances.

It is evident from a review of the literature that India is considered to be one of the chief sources of infection, but it is not at all certain that Lower Bengal and the valley of the Ganges is the one and only endemic centre which it has been commonly supposed to be. Fayrer and Corré are probably more nearly correct in their estimate of the danger spots in the Indian peninsula. Indeed, if the conditions of air, water and soil in the Ganges valley make that area "the home of cholera", it will not be difficult to name a score of other areas in which identical conditions may be found; and it seems more reasonbale to adopt Herbert's view that cholera "is very generally endemic in some degree throughout the greater part of India". Experience in the past few years compels one to be very diffident in deciding whether a given area should be classified as endemic or not, especially now that the question of chronic "carriers" has been shown to be so important.

As regards other countries, Tholozan would seem to have proved that Central Asia may be included in the list of endemic centres or "points d'emergence". Similarly, the Shat-el-Arab area may be included, and the experience of the last twenty years or more would also seem to point to one or more foci in Southern Russia, particularly the shores of the Black Sea, the Volga Valley, and, as Simpson suspects, certain localities near the Caspian Sea. Only one authority has named Egypt as an endemic centre, but the necessary evidence is doubtful, and it may be left out.

In addition to these, we may include the Federated Malay States (especially Kedah), Java and the Dutch East Indies, Indo-China and the Philippines. There is little or no evidence on record implicating Southern China, although that area must be looked on with suspicion. The references to Japan apparently exclude that country.

The more one studies cholera from this point of view, the more difficult and confusing does the issue become, for, voluminous as the literature is, it cannot be said to throw any very clear light on this vexed question. Little of the available evidence is scientifically accurate, and a great deal of detailed and painstaking research will have to be done before a more definite opinion would be justified.

CHOLERA-CARRIERS

During the last ten to fifteen years a considerable amount of time has been devoted to the investigation of the "carrier" problem.

McLaughlin [24] notes that Pfeiffer has found bacilli in the stools of convalescents up to 69 days. In Bilibrid Prison, Manila, he found 17 carriers, or 6.44 per cent, in 264 healthy persons living in infected areas, and cholera-carriers less dangerous than typhoid-carriers, as they did not void bacilli in the urine and usually carried for much shorter periods.

Dr. Crendiropoulo [25] finds that agglutinating vibrios are only found in travellers from infected countries and only when an epidemic is at its height. During the decline of an epidemic, carriers become extremely rare, and both agglutinable and non-agglutinable vibrio carriers cease altogether when an epidemic comes to an end.

Jatta [26] states that the organisms found in carriers were no less virulent than those isolated from actual cases, but were present in smaller numbers.

Henri Poitevin [27] found that 97 per cent of his carriers were free at the end of a month. It appeared highly exceptional to carry the germ for more than two months. "Carriers were much more common in a group of poor and destitute pilgrims than in those of another group much better off."

Greig [28] found the comma bacillus living in the bile and in the wall of the gall bladder, ideal conditions for a prolonged life; and this afforded an explanation of the mode of production of the "chronic carrier". Anyone harbouring the bacilli in his gall bladder is a reservoir of the virus and is liable to produce fresh epidemics. At Puri, in 1912, 27 contacts examined showed six excreting cholera bacilli in their stools and these individuals were apparently quite healthy at the time. He also found that 36 per cent of the recovered pilgrim cases discharged from Puri hospital during the Jagannath festival of 1912 were cholera-carriers, and that a number of attacks took place in the Central Provinces after their return.

Greig [29] also showed that a "carrier" not only caused an epidemic of cholera among gaol prisoners but produced two cholera-carriers, and these may become "permanent reservoirs" of the virus. "In a free population, where no precautions would be taken for the segregation of 'carriers' produced by an epidemic, the situation is a dangerous one. After each epidemic there must be a crop of 'carriers', some temporary and some permanent, who will, if suitable conditions offer, produce outbreaks of the disease in the same manner, and so the vicious circle of events continues."

Job [30] gives a careful summary of all workers on cholera as regards "carriers", both healthy and convalescent, chronic and ill, from the date of the discovery of the bacillus up to 1913. That healthy carriers exist he proves conclusively from his

search through the literature, mentioning as he does dozens of papers. He also discusses whether the "El Tor" bacillus, which was found in healthy carriers, was really a cholera bacillus or, as KRAUS and others said, was a *vibrion paracholérique*, but he agrees that it was a real cholera bacillus. He also speaks of the persistence of the vibrio in fæcal matter. FILOFF recovered the vibrio alive in excrement of cholera patients during 101 days. RABESCHA once found it for a period of nine months. In latrines mixed with water, FÜRBRINGER has noted that the vibrio can live for 106 days.

HEISER ([31]), in dealing with sporadic cases in 1913, found cholera bacilli in the stools of the contacts in many instances. No cholera had been recorded in the Philippines previously since October 1911. There was considerable evidence that cholera-carriers may always be present in the Philippines and that perhaps the organism passes through a cycle, during certain stages of which it may not be recognisable by laboratory methods.

GREIG ([32]) once more emphasises the carrier as the important individual, as the vibrio is excreted only intermittently in the stools. Cholera vibrios are also to be found in the urine.

The League of Nations Commission ([33]) found a very high carrier rate in the foci of infection in Poland in 1920.

In connection with the same subject, the term "latent" is used by more than one writer. In El Tor ([34]) six cases dying of dysentery and colitis were found to have comma bacilli in their intestines, and these were later proved by agglutination to be true cholera bacilli. The persons were obviously carriers of cholera, and patients have been shown to keep the vibrios for over two months after recovery. "The bacilli were apparently modified in such a way as not to produce cholera in the persons harbouring them, but had they lost all power of producing cholera or might they in certain circumstances have possessed or regained that power?" The presence of such persons presents a very serious problem, as in the case of the Mecca pilgrimage.

Dr. Paul CLEMENTS ([35]) is of opinion that "in the Philippines the typical incidence curve usually follows the importation of a virulent case into a previously healthy locality, while the type of incidence last mentioned is as if there was a widespread 'latent' infection, *i.e.*, of carriers, some of which, from causes not yet entirely understood, develop into cases."

The "cholera-carrier" has now been justifiably recognised to be of the most vital importance, not only in connection with the spread of infection, but also as regards the carrying-over of the infecting germ from one favourable season to the next. A "carrier", no doubt, voids the comma bacillus only periodically, but in endemic areas like India, where the disease is so widespread, many thousands of these individuals must exist at any one time, and, as has been proved in the Philippines, must be constantly present. These are the persons responsible both for the small

and limited, often unreported, outbreaks experienced during the non-epidemic seasons of the cholera year, and also for the large recurring epidemics and pandemics.

It is not necessary to theorise on the conditions of soil and water best suited for the growth and multiplication of the bacillus. The gall bladder of the human "carrier" is a much more convenient nidus for the continued life of the germ, and the "vicious circle" of events described by Greig without doubt is carried on in this manner. Observations already made show that the vibrio may be found for as long a period as 106 days in the human intestine. Greig talks of "permanent carriers", and there does not seem to be any reason why a cholera "carrier" should not permanently carry the *vibrio choleræ* if a typhoid "carrier" may go on excreting *B. typhosus* for life.

The cholera "carrier" may therefore be said to constitute one of the most serious problems in connection with the spread of the disease along the routes of travel, whether international or not, and this discovery has made it easy to understand how cholera appears in such haphazard fashion, passing by one place and springing up in another without apparent plan or reason. The "latent" infection being always present, it only requires "the suitable conditions" referred to by Greig to convert the latency into a fresh outburst of the disease. Later sections will indicate how some of these suitable conditions may arise.

PANDEMICS.

Whatever opinion may be regarding the endemic foci for cholera, there seems to be no doubt but that the disease is characterised by periodic pandemics, at times spreading all over the world before it once more dies down.

Fayrer (4) mentions Hirsch's *Handbook on Geographical and Historical Pathology*, which describes a series of pandemics. These are tabulated as follows:

Period	Entrance into Europe
1817-23:	India to Russia in 1822.
1826-37:	India (*a*) to Mesopotamia, Arabia, Syria, Palestine and by Suez to Egypt and Africa; (*b*) by Persia and Transcaucasia to Russia and Europe.
1846-63:	Widely prevalent in India, and spread by the same two routes as above.
1865-75:	From India west, (*a*) from Arabia to Suez, Malta, France, Spain and Italy, an unusual route; (*b*) Turkey to Europe, then later Persia, Mesopotamia, and a remission in 1869-70, except in Russia and Persia.
1883-87:	Cholera restricted to Egypt, Toulon, Spain; later in Russia.

Simpson ([21]) describes nine invasions of cholera into Europe within a period of little more than ninety years. These have varied considerably in duration, power of diffusion and severity, the more lengthy ones having important recrudescences.

Period	Entrance into Europe	Interval between each invasion in years	Number of years in Europe	Spread of infection
1823	Astrakhan	—	Less than one year	Not further west. Persian and Turkish armies suffered.
1830-37	Astrakhan	7	7	Very virulent among Russian and Polish troops. Also great epidemics among Mecca pilgrims.
1847-52	Astrakhan	10	6	Severe and widespread. Invaded a larger world's surface than that of 1830-1837. Also epidemic at Mecca.
1852-59	Astrakhan	Nil	8	More severe and widespread than previous epidemics. Persia severe, Crimea severe. French troops in Algeria and Spanish troops in Morocco infected.
1865-68 (in Russia until 1874)	Constantinople and Southern ports of Europe.	6	10	Severe but more limited in diffusive power.
1884-87	Marseilles and Toulon.	10	4	Less severe and limited.
1892-96	Baku	5	5	Less severe and limited.
1905-12	Baku and Astrakhan	9	8	Mild and limited.
1912	Constantinople	—	—	Mild and limited. Turkish, Bulgarian, Greek and Serbian troops.

Greig ([32]) describes seven pandemics. "In the first pandemic, the infection was carried from India to Mecca in 1831".

1. 1826-37 . . . . . 11 years
2. 1840-49 . . . . . 10 „
3. 1853-56 . . . . . 4 „
4. 1863-68 . . . . . 6 „
5. 1868-73 . . . . . 6 years
6. 1881-85 . . . . . 5 „
7. 1892-94 . . . . . 3 „

"In the seventh pandemic the speed of transport had greatly increased, taking months instead of years to accomplish the journey from East to West."

Simpson perhaps gives the best analysis of these pandemics, and, as the other two writers more or less corroborate his dates, we may take it that his record of events is substantially correct. The 1912 pandemic certainly continued in Europe up to 1916, and although, as Simpson states, it was mild and limited at first, the clouds of war later prevented any clear vision of the course of the disease in Eastern Europe, and it is probable that infection was more severe and widespread than was commonly thought. A tenth pandemic occurred during the years 1918-1922, when the disease existed in a very severe form in Russia and Poland. How this infection was initiated is by no means clear, and the question arises as to its possible inception in some parts of Southern Russia. It cannot be said that the intervals between the different invasions reveal any regular periodicity, although in no instance has the interval been less than five years. From this point of view, therefore, we are no nearer a solution of the question as to the factors responsible for these periodic pandemics.

ROUTES OF SPREAD TO THE WEST.

Much time and labour have been expended in the past in investigating the routes along which infection spread through the East and to Europe, and the references in the literature are many and varied. Considerable space has been allotted to an analysis of these papers, and, in particular, a detailed description is given of the spread of the disease from 1902 onwards in the hope that some final conclusion might be reached.

Willoughby ([11]) states that the well-marked routes of spread of cholera are: (*a*) Central Asiatic, (*b*) North Persian, (*c*) Persian Gulf, and (*d*) the Red Sea.

Nothnagel ([5]) writes that "cholera can occur in a locality outside of India only if it has been introduced there". Epidemics always follow the lines of travel.

In 1826 ([4]), the pandemic which began in Bengal travelled to Russia, thence to Europe and England via Riga and Hamburg. The infection in the 1846 pandemic travelled via the Caspian Sea in 1847 to Russia (1848) and to England (late 1848), probably by Hamburg. In 1853, cholera came to Europe again by the same route and to England by Hamburg, but the fourth pandemic route was governed by the Suez canal construction, the disease for the first time being carried from Mecca to Suez by pilgrims, thence to the Mediterranean and to Northern Europe.

([53]) In 1883-84, attention is drawn to an extensive and fatal epidemic of cholera in Egypt, beginning in June at Damietta.

Thorne describes an epidemic in Italy and Malta in 1887. Italy had suffered severely in 1884-86, and still more so in 1887.

Cholera died down in Europe in the winter of 1892-93, but persisted in some parts of European Russia and in Yemen, in Arabia. To this last is due the epidemic of Mecca pilgrims with 30,000 deaths, and by them carried to Asia Minor, Turkey-in-Europe, Tripoli and Morocco. Western Russia suffered severely, and recrudescences appeared in Holland, Belgium and Germany. Hungary became widely invaded, as did Austria and Bosnia. Italy and Spain were infected later. In Western Asia, where the disease was probably related to a previous diffusion in Persia, a severe outbreak occurred in the vilayets of Basra and Baghdad.

Dr. Barry states that in 1893, as in 1892, there were two independent diffusions of cholera in the Ottoman Empire, one a continuation of the epidemic which prevailed in Arabia during 1890, 1891, and 1892, and the other affecting Mesopotamia and confined to that province. A large epidemic occurred in Persia, with 150,000 deaths, due possibly to fresh importation from Mesopotamia. Very few cases occurred in Russia during the winter of 1892, but with warmer weather cholera again became very active. In 1892, there was great intensity in the Caucasus and in the Volga provinces, but, in 1893, the Ukraine or borderland provinces were infected, because in 1893 there was no march west of imported infection but only a series of recrudescences in a number of provinces.

During the same year, Senegal, Algeria (a recrudescence of previous cholera), Belgium, Tunis, the Netherlands, Roumania, the United States, Egypt, Brazil, Tripoli, Morocco, Spain, Serbia, Sweden and the Canary Islands were all infected. A number of German reports by Pfeiffer, Kohlstock, Passow, Reincke, Frosch, Freidhein, Von Esmarch and Wutzdorff and Austrian reports by Dr. Daimer are quoted. All these investigators showed cholera infection to be spread by water *e.g.*, wells and river-water supplies. The report closes with certain conclusions:

> "(*a*) Diffusion of cholera has invariably followed lines of human intercourse; (*b*) increased facilities for steam communication by land and water, especially between Central Asia and Europe, have conduced to a rapidity in the diffusion of cholera hitherto unprecedented; (*c*) all explosions of cholera have been found to have been referable to specifically polluted water supplies, and (*d*) cholera in its progress by way of river traffic has fastened on more centres of population than when its diffusion has taken place over land."

The prevalence of cholera in 1894 was only due to local continuations from 1893, and to recrudescences. Russia was the main centre in 1894 and 1895, more especially those provinces adjoining the frontiers of Austria and Germany. Galicia also had epidemics in 1894 and 1895. Winter epidemics occurred in Turkey in 1893-94 and 1894-95. There was no cholera in the Hedjaz in 1894, but in 1895 a large epidemic took place, which spread to Egypt and Morocco. In the summer of 1896, 20,000 deaths occurred in Egypt. "It is not India which is a standing danger to Egypt, but her own pilgrims"

In connection with the epidemic of cholera in Egypt in 1902, Proust [17] insists that cholera coming from India follows only two paths. One, observed in 1823, 1830, 1847 and 1892, is the land route either through Afghanistan or Persia and to Europe by the Caucasus and Russia; the other, the sea route by the Red Sea and pilgrims from Mecca, and more or less directly to Egypt, and thence to the whole basin of the Mediterranean, as observed in the epidemic of 1865. The epidemics of 1865, 1883, 1895 and 1902 were all imported, three from Mecca, and one directly from India. In 1865, the epidemic in Egypt was the source of the invasion of cholera into Europe. In 1883 and 1895, Egypt was not invaded, but, he adds: "... the protection of Egypt is not a local matter but is one for the whole of Europe ".

Onitzkanski [36] says that Russia was free from cholera from 1896 to 1902, but the disease broke out in that year in Siberia. Coming from Manchuria in June 1902, it reached the province of the Amur, but it was not till 1904 that cholera was imported into the Empire from Persia, where, early in 1904, it had been brought from Baghdad. He admits that the propagation of cholera in Siberia and in some of the provinces of Central Asia is due to immigration movements.

Regarding the Hedjaz epidemic of 1902 [37], all that is clear is that the stream of pilgrims to Mecca from all parts of the Moslem world brought cholera infection to Hedjaz from some undetermined endemic centre in the East, and that it was responsible for the two years' prevalence of the disease. During the fifteen preceding years, the disease had appeared among Mecca pilgrims four times only — 1890, 1891, 1893 and 1894-5. In 1900, the deaths in India were the highest ever recorded, but the first Western extension was not that in the Hedjaz but that in the autumn and winter of 1899 when a severe epidemic occurred at Basra, on the Shat-el-Arab, and in Mesopotamia. A very severe epidemic appeared in Oman, in South-Eastern Arabia, at the same time, and this outbreak was believed to have been very probably derived from the opposite coast of Makran, whence it was thought to have come direct from Karachi. It has been surmised also that the Hedjaz infection of 1902 may have been carried by pilgrims and travellers from Oman, and not by direct importation from India, but, as the Oman outbreak died out in the summer of 1900, probably this is not so.

It is not certain [18] what was the source of the cholera which broke out among the Mecca pilgrims in 1902, but it is said to have been brought from Java in a pilgrim ship, though it may have come from India by land in caravans from Mesopotamia. From the Hedjaz the infection was carried to Egypt, almost certainly by returning pilgrims, thence to Syria, and, following the lines of communication, spread to Damascus, Aleppo, the valley of the Orontes River, the valley of the Euphrates, then to the Tigris valley, and before the end of the year to Mosul and Baghdad. In Yemen, in South-Western Arabia, cholera broke out one month after the Hedjaz outbreak, having been infected by returning pilgrims. During the two years 1902-04, the disease prevailed throughout the Turkish Empire, but in no part was it one of remarkable severity or long duration. Bruce Low adds that there was hardly any in Egypt,

Palestine and Mecca, but Syria suffered considerably and the infection travelled East to the Euphrates and to the Persian Gulf.

From March to June 1904 ([38]), cholera extended markedly to Mesopotamia and Irak-Arabi, and also into Persia, *i.e.*, Kermanshah, being carried there also by returning pilgrims. In June, a serious extension of the epidemic occurred in Persian Kurdistan, while it was not diminishing on the Turkish side of the Turco-Persian frontier. In Persia, cholera became quickly prevalent, and in July 150 deaths a day were taking place in Teheran. In September, Meshed, Resht, Astrabad were infected, and a case was reported in Baku later the same month. Tabris and Maragha, near the Transcaucasian frontier, were infected, and Enzeli, on the Caspian Sea, and Merv, in Transcaspia, also reported cases in August. By the end of September, Baku had suffered badly, and Saratot, on the Volga, was also infected. Erivan, in Transcaucasia, was severely infected in November, and in December reports of considerable recrudescences in Asiatic Turkey were made. By December, cholera was prevalent in Eastern European Russia. The same route into Russia was taken by the disease during the epidemic in 1892.

Towards the end of December 1904, cholera appeared in Van, Armenia. By May 1905, the epidemic had died out both in Russia and Turkey. The Constantinople Board of Health report states that the epidemic spread along two main routes, from Kerbala, one route north and east through Baghdad and Kermanshah to Teheran and Eastern Persia; and the other, south to Basra and the shore of the Persian Gulf. The first route was infected by caravans of pilgrims.

Early in 1905, cholera spread to Volhynia and Poland ([40]), "a route which previous experience has shown to be dangerous to the whole of Europe". The disease in Germany was confined mainly to the provinces of East and West Prussia and Posen, and in Galicia in Austria, *i.e.*, all round Polish Russia. In 1904, cholera ([39]) was introduced from Russia by the river craft and followed the course of the inland waterways with the floating rafts down the Vistula from Poland, through the canals into the Oder via Havel and Spree, and thence by canals to the Elbe.

The epidemic of 1904 in Persia continued up to April 1905, and to a lesser degree in Russia during the whole of 1905, but ([42]) from February 1906 to July 1907 a cholera-free interval was experienced in Russia and Turkey. A widespread but not severe epidemic then began on the Volga, which spread to most parts of European and Asiatic Russia, and thence to Asiatic Turkey and Persia. The disease again broke out in the Volga valley in 1908 and spread widely. Bruce Low ([43]) states that, during the Haj of 1908, it was estimated that 21,000 deaths occurred in the Hedjaz. During 1909 and 1910, cholera was again widely prevalent over Russia, both Asiatic and European, and towards the latter half of 1910 infection was reported in Constantinople and in both European and Asiatic Turkey. A widespread epidemic occurred in Turkey in 1910, and ([44]) undoubtedly "the infection was imported on a number of occasions from Russia by ships or by travellers across the land frontiers in Asia Minor".

Chantemesse and Boul ([45]) deal with cholera from 1904. In 1907, they say that cholera reappeared in the Hedjaz among pilgrims arrived from Russia, or perhaps by those who came from India. They hold that "cholera spreads: (*a*) by propagation, slowly passing step by step from one place to the next, a dangerous mode of extension as the carrier is unknown; and (*b*) the transport of cholera by a ship or a train, by healthy carriers it may be ".

The Haj became infected by Java pilgrims in December 1910 ([44]) and, in January and February 1911, returning pilgrims in Asiatic Turkey caused continued cholera cases and deaths. Cholera persisted in the Hedjaz and in Yemen, though Russia was free for three months from February to May. In August, cholera broke out in Turkey and Italy, and spread to other countries from there, but, except for an outbreak in the Volga basin and a few scattered cases near Minsk on the borders of Poland, little was reported from Russia, and it appears as if the "virulence of the cholera germ were becoming exhausted " in Russia.

Italy suffered worst in 1911, but Malta and Tunisia also reported bad outbreaks. Infection was brought to Algiers and Port Said by ship by refugees from Malta.

In 1911 ([46]), Asia Minor was widely infected, as was Mesopotamia: in the summer, a severe and prolonged epidemic took place in Basra and the outlying districts. A severe outbreak occurred in Constantinople. In January 1912, the disease was still present in a few places as widely separated as Albania, Asia Minor, Syria, Palestine and the Yemen, as also Aleppo.

During the summer of 1912 ([47]), several ships from Bombay arrived at Camaran infected, and this must be associated with the serious epidemic which was then raging in that city. In October 1912, reports state that, for the first time for many years, cholera seems to have been absent from the Russian Empire. The Hedjaz has been infected from two sources: (*a*) from the north, *i.e.*, Damascus and Syria, where the remains of an epidemic that has prevailed for several years still exist; and (*b*) from the south and west a fresh strain newly imported from the homes of the disease in the Far East. Cholera still existed in Ahwaz (Persia), and a considerable epidemic among pilgrims from the Hedjaz occurred from October to December, whilst the disease was also reported in Jeddah and in El Tor. Egypt was free from the disease. Freise gives ([48]) a history of the spread of cholera from 1899 to 1911, but beyond mentioning the places infected, his sole endeavour seems to have been to trace the source of cholera from India and to show its path westwards.

A few cases were reported from Odessa in January 1913, and a severe outbreak occurred in the Tchatalja lines from November 1912 to February 1913. In September Bulgaria, Serbia, Greece, Roumania, Austria-Hungary and South Russia were all infected, but were again free before the end of the year. The disease was introduced by emigrants to Smyrna, as also to Scutari on the Bosphorus. After September, cholera rapidly declined in the Turkish Empire and disappeared early in November. In South Russia, infection was fairly extensive but nowhere severe, and died out in November. The Constantinople outbreak was also mild ([49]), "all pointing to the belief

that the virulence of the virus was gradually dying away ". A revival took place in July 1914, and became more seriously extensive later in the year.

In 1914, Russia and Austria were infected and there were sporadic cases in Warsaw. Turkey also reported cases in 1914. Germany was infected in 1914 by Russian prisoners. Cholera appeared among the wounded in Austria in September 1914, and the infection reached Vienna.

In September 1915, it was reported that 20,000 cases had occurred in Austria, mostly in Galicia and Bukovina, but the disease was also present in Croatia-Slavonia, Bosnia and other parts. Prussian Silesia, Posen and Pomerania were also infected, and by the middle of the year the disease reached Italy, *e.g.*, Leghorn and Venice.

In 1916, Syria and Mesopotamia were known to have been infected, and during 1917 Asia Minor, Syria and Mesopotamia suffered, and there were a few cases in Egypt. War conditions favoured the spread in Eastern Europe, and the ravages of the disease were probably greater than were reported. News from Russia was very scanty, but (50) that country was infected continuously from 1914 to 1918, although no details are given. In 1918, cholera was reported from the city and district of Petrograd, from Middle Russia, the Lower Volga and Astrakhan. In Asiatic Russia, it was prevalent in May 1918, in Tashkent, and cases were carried to Stockholm and Christiania. In Turkey, there seems to have been a cholera-free interval for over two years in 1917-18, but in August 1918 a slight outbreak occurred. During 1919, cholera caused little trouble in Turkey, but in the latter half of that year South Russia and the Crimea were severely infected, as were parts of the Volga basin. In 1920, the epidemic increased in gravity, particularly in the Don basin and Koursk. Cholera was reported (51) in Poland in September 1920 amongst Russian prisoners of war.

During 1921, the outbreak in Soviet Russia became more alarming, 136,000 cases being reported, and, whilst affecting the same regions as in previous years, it was most severe in the Volga provinces and in Siberia. Only isolated cases were reported in Moscow and the West. The epidemic subsided during the winter, but a focus of infection remained at Rostof-on-Don, and in 1922, whilst cases were fairly widely diffused throughout Russia, the Ukraine, suffering from famine, experienced a very severe outbreak, most towns on the Black Sea littoral being affected. The City of Odessa became contaminated in April, and suffered terribly until the epidemic was controlled in August. A few cases of cholera reached the Polish frontier quarantine stations during the summer. Mecca remained free in 1922 (52).

Bloch (54) writes that the recent cholera epidemics are traceable to 1904, when infection was introduced from Persia through Transcaspia. The eighteen-year chain of epidemics that followed is divided into two periods, 1904-13 and 1916-22. The first period reached a maximum in 1910, and in 1912 fell to a minimum. By 1918, the epidemic again rose high, but in 1921 Russia experienced one of the severest outbreaks of cholera, second only to that of 1910. The author says that the disease spread along routes of travel by contact (?) and no infections were traceable to water.

PILGRIMAGES, FAIRS AND RELIGIOUS FESTIVALS.

The effect of pilgrimages, fairs and religious festivals on the spread of cholera must also be noted in the same connection.

Duncan (84) writes that India is the land of sacred pilgrimages. In 1867, at Hurdwan, cholera broke out and was spread in every direction by returning pilgrims for 50 to 300 miles. Human intercourse plays a very great part in the diffusion of the disease, and returning pilgrims are very dangerous arrivals. In the North-West Provinces it has been shown that cholera epidemics have become more frequent since the introduction of railways.

Professor Hirsch, of Berlin, says: "That it is human intercourse which furnishes the media for this communication is proved on a large scale by the observations on the diffusion of the disease by pilgrimages and military campaigns both in India and beyond it; while there are other conclusive proofs furnished in innumerable instances from the smaller circles of diffusion."

Clemow (37) writes: "All that is clear is that the stream of pilgrims from all parts of the Moslem world to Mecca brought cholera to the Hedjaz from some undetermined source, and that this was responsible for the two years' prevalence of the disease" (1902-04).

Bruce Low (50) confirms this in the following words: "In the past, the great religious fairs and pilgrimages have played a prominent part in the spread of cholera."

Proust (17) writes: "In awaiting the departure of the ships from Bombay, the pilgrims get infected, carry the disease on board and propagate it far and wide."

Hart (13) says, regarding pilgrims: "There should be a rigid examination of all pilgrims at the starting-off points, and the weak should be weeded out."

Legrand (85), recognising the danger pilgrims are to Egypt, recommends that one year's pilgrimage should be reserved for India and the Far East, and another year for Egypt and the West.

The report of the Pilgrims' Committee (86), appointed by the Government of India, proves conclusively, by numerous instances, the importance of pilgrim centres in spreading cholera all over India.

Clemow (59) says: "The spread of cholera in Russia is much facilitated by the habits of the population, as, for example, the migration in the spring of large bodies of peasants to the south and east in search of employment and the periodical bazaars and fairs which are a marked characteristic of Russian life."

The first point which attracts attention is the frequency with which Mecca is mentioned as the great centre for the spread of the disease. Whatever the primary source of infection may have been — and in many instances considerable doubt

exists on the matter — pilgrims from Mecca have constantly been the means of spread of cholera. Travelling along the main routes, the disease has been carried to Syria and Asia Minor and from thence to the valley of the Euphrates, to Persia and to Transcaspia and Russia, and, on the other hand, either directly from Mecca to Egypt via Suez, or indirectly from Syria to Egypt and thence to the shores of the Mediterranean, both north and south. No shadow of doubt remains regarding the danger of the Hedjaz as a centre from which cholera is spread, and Ernest Hart ([13]) was justified in his indictment of this plague-spot and in his opinion regarding the vital necessity for its sanitary control.

It is, however, by no means certain that Mecca is always directly infected from India. In 1902 and again in 1910, pilgrims from Java are said to have been the source of the disease, whilst infection was imported on more than one occasion by travellers from Russia and from Damascus and Syria. In the winter of 1892-93, again, the disease was carried from Yemen in Arabia, causing 30,000 deaths among the Mecca pilgrims, and other instances are quoted where the disease was probably brought in by caravans from Mesopotamia. From the records, however, it is apparent that Mecca provides the "suitable conditions" which Greig finds necessary for fresh outbursts of the disease where "latent" carriers are present, and, when one remembers the numerous endemic areas from which the crowds of Mecca pilgrims are drawn, it is not difficult to understand why the Hedjaz should be the danger to the world it has been shown to be.

This fact seems to be of far greater importance than that cholera infection usually spreads via North Persia to Transcaspia and thence to Russia and to Western Europe. The disease travels just as easily — more readily, indeed, within recent years — via Egypt to the littoral of the Mediterranean and by the Hedjaz Railway to Asia Minor, and, with more rapid and modern means of transport, the latter route has become the more dangerous one. It must be reiterated, however, that routes of spread are of minor importance. It is nothing new to say that cholera travels along the trade routes. That fact has been known for many years. *The* important factors are: (*a*) the presence of "carriers"; and (*b*) those suitable conditions which make the "carriers" a grave danger to the whole world.

ROUTES OF SPREAD IN THE FAR EAST.

In any discussion on the epidemiology of cholera, it is just as important to consider the spread of the disease in the countries of the Far East as it is to study the routes of travel to Europe and the West, but the literature, immense as it is, contains few references to this part of the subject.

Bruce Low ([50]) says that, from 1896 to 1917, or in a period of twenty-two years, 8,256,832 people in India are said to have died of cholera. During 1914-17 also, French India, Ceylon, the Dutch East Indies, the Federated Malay States, Siam

and Indo-China had 16,743 deaths, with a 70 per cent mortality, and the disease existed also in China, Formosa and Japan.

Freise ([48]), in his paper dealing with the world spread of cholera from 1899 to 1912, says an epidemic began in India in 1899, but Burma, Siam, Java and Saigon were also infected. In 1900, there was a greater spread in India, and Singapore became infected. In 1901, Borneo, the Celebes, Java and Sumatra reported the disease. In 1902, it became widespread in the Far East, China, Canton, Manchuria and in Japan, and was also very widespread in Transbaikalia. By 1903, the Philippines had become badly infected, though it was less severe in China and Japan, but worse than 1902 in French China. In 1904, the Philippines were severely stricken and Cochin-China, Port Arthur, Shanghai and other Chinese ports were also badly infected. In 1905, the disease was severe all round the Indian sea-board, and was also present in Moulmein and Manila. In 1906, the infection was still severe in British India, very widespread in Ceylon, and the Philippines and Bangkok, Singapore, Hong-Kong and Shanghai were all infected.

In 1907, the disease was still present in Bangkok, Manila, a few additional towns in China, in Manchuria and Korea, and fairly widespread in Japan. In 1908, the Straits and Singapore and scattered towns in China still reported cases, and the disease was severe in the Philippines. In 1909, Siam, Indo-China, Korea (in severe form), Japan, the Philippines (where an epidemic raged), the Dutch East Indies (in epidemic form), especially Java and Sumatra, were all infected. In 1910, Singapore, Bangkok, Siam (in epidemic form), Cochin-China, Annam, Hong-Kong, Manchuria (where it was widespread), Transbaikalia, Japan (particularly Kobe and Osaka) and the Philippines were still reporting the disease, and in 1911 it persisted in the Straits, the Philippines, Hong-Kong, Japan, and in Siam.

It may be noted here that the epidemic in the Hedjaz in 1911 is said to have been brought from Java in pilgrim ships. During this year, the disease was probably more widespread over the whole world, Western and Eastern, than it had ever been before. Whilst in these Far Eastern countries cholera had existed for a considerable number of years, no clue is given by Freise ([48]) in his paper as to whether India was to blame for the primary infection; but as he traces the source of cholera from India in respect to its presence in Western countries, it is probably fair to infer that he would also blame India for the widespread infection found in the countries of the Far East.

During 1912 ([56]) India was very widely affected, being worse in Bombay. The Straits and Singapore, Bangkok, French Indo-China, the Dutch East Indies all experienced an epidemic, as did Formosa, China and Japan, China being particularly affected. No cholera was reported from the Philippines. In 1913 ([57]), Ceylon, the Malay Peninsula, Bangkok, Indo-China, the Dutch East Indies, Formosa and Japan were still infected, and China suffered from a widespread epidemic.

Japanese workers are unanimous in asserting that cholera is not endemic in their country, but is always imported. On the other hand, Heiser ([31]) and other American

writers admit that the disease is probably endemic in the Philippines, and Hoops (23) in 1916 seems certain that parts of the Federated Malay States are also endemic foci.

It is to be noted that the infection in most of these Eastern countries was first reported from the large ports, which would seem to point to an importation of the disease. At the same time, it must be remembered that it is possible that primary outbreaks took place in the interiors, and reports were only made when the disease reached the international ports. There is reason to believe that cholera is not endemic in Siam, while, on the contrary, parts of the Dutch East Indies are known to act as endemic foci for the disease.

Conditions in China, especially in Southern China, are such that there seems to be no reason why cholera should not be endemic there. Unfortunately, the literature on the subject contains no reference of value. The Local Government Board reports on cholera are entirely silent as regards most of the Far East.

In the light of available evidence and our present-day knowledge, it is difficult to believe that the countries of the Far East only become infected with cholera when the disease is imported from India. In several of the Far-Eastern countries, endemic foci have been shown to exist, and, when suitable conditions arise, the permanent "carriers" are just as liable to produce an outburst of cholera there as in India itself. Careful investigation, such as has been carried out in the Philippines, corroborates this view. Because of the numerous trade routes which are met with in the Far East, it is difficult to trace any definite path of infection, but it may be justifiably assumed that those sea-routes are responsible for the spread of the disease from the endemic centres scattered over this vast area.

CLIMATIC CONDITIONS.

Climatic Factors in General.

Smith, E. (62), writes that cholera in India prevails at the season of the year when there has been a very small fall of rain, large accumulations of electricity in the atmosphere and a prevalence of south-westerly winds of small force. These, in addition to heat, produce a sultry atmosphere which tends to induce exhaustion of mind and body. Bad water, sewer gases, and decomposition of animal and vegetable matter also help.

Bellow (2) says:

> "Records afford evidence of the existence of an undoubted relation between the meteorology of a place and its liability to cholera activity. The principal features are: (*a*) an unusually high day temperature; (*b*) excess in normal humidity of air; (*c*) a more or less complete stagnation of air; (*d*) a general muggy oppressive atmosphere; and (*e*) most important, an unusually high range in the diurnal temperature, *i.e.*, between the temperature of the air during the day and night. The characteristic features

of climate attending the respective seasons, and present in the areas of cholera prevalence, are heat and humidity of the atmosphere, combined with an active evaporation from a more or less moist soil, and an excessive range of day and night temperatures. In India we find that the seasons most favourable to the general or epidemic prevalence of cholera are both the hot-weather and cold-weather monsoons in Southern India, but only the hot-weather monsoon in Northern India. The facts are that seasonal changes of weather producing unusual excess of temperature and humidity of air and soil, with consequent activity of evaporation from the soil, and with the resulting day and night alterations of temperature and chill, are the invariable concomitants of cholera activity.

"When the conditions of weather and soil are such as to reduce to a minimum the evaporation of moisture from the soil, with its accompanying changes of temperature and humidity in the air, then the activity of cholera is also at a minimum. But when the conditions of weather and soil are such as to raise to a maximum of intensity the evaporation of moisture from the surface of the soil, with its accompanying sudden alterations of temperature and humidity in the air, then the prevalence of cholera also acquires a maximum of intensity. The activity of the evaporation of moisture from the surface of the soil depends in the first place on the temperature of the air, and in the next on the amount of moisture in the soil, an excess amount of moisture, to the extent of submerging the soil under water, being prohibitory of free evaporation. Hence the greater activity of cholera in Bengal and similar moist-soil tropical countries during the autumn and winter months, and its almost entire abeyance during these seasons in the dry-soil extra-tropical Punjab and Central India. The normal winter heat of South India is favourable to the free and rapid evaporation of the surface-soil moisture, and we therefore find regular manifestations of cholera during the winter months.

"The great difference of the prevalence of the disease in Europe and America and in India is the striking regularity of its periodic recurrence in epidemic form in India. But this is only confirmatory of the view that the disease depends for its origin, as well as its epidemic development, upon influences of weather; for in no other country is the succession of seasons marked by meteorological phenomena of such magnitude and violence, or by such sudden and great change in the conditions and states of the weather elements, and with also such regularly recurring periodicity, as they are in India."

Moore ([63]) says that "certain meteorological phenomena have most generally accompanied outbreaks of cholera, the chief of which conditions have been found to be a somewhat variable but elevated temperature, a still and peculiarly oppressive state of atmosphere, more oppressive than simple elevation of the

thermometer can account for, conjoined with a certain degree of moisture and frequent absence of ozone ".

Willoughby ([11]) maintains that the cholera microbes in Bengal perpetuate themselves in the soil; in the other provinces of India, they remain dormant in the soil, ready to break forth into activity at various intervals depending on seasonal conditions or aggregations of human beings.

Herbert ([64]) concludes:

> "(*a*) There is a general rough correspondence in the curves of atmospheric pressure variations and of annual cholera prevalence; (*b*) when hot-weather pressure is below normal, little or no cholera exists, but a high hot-weather pressure is found in heavy cholera years; (*c*) exceptionally heavy rainfall in the North Deccan may occasionally increase cholera there so much as to vitiate calculations based on pressure alone. In Madras Presidency, the connection between pressure and cholera is nearly as close as in Bombay Presidency. Again, in Madras Presidency, drought in the earlier monsoon is favourable, and excess unfavourable, to cholera prevalence. The influence of the north-east monsoon appears quite subordinate to the other. It is curious that, in the south-west monsoon, a time of light rain in the Carnatic, excess should be fatal, while later in the year, when the heaviest rain falls in October and November, excess is favourable. But the cold-weather cholera does not usually attain any intensity until the rain is over. "

He admits that the theory of atmospheric pressure does not work for Madras Presidency, and in his second article he fails to prove his case.

Herbert ([16]) refers to two types of cholera outbreak, the one attaining its maximum at once, the other rising gradually. "Is not the former typical of an importation from without under conditions unsuited to the continued development of the organism, and the latter characteristic of multiplication of the indigenous organism under increasingly favourable natural conditions ? Rainfall, temperature and atmospheric pressure influence cholera. Provinces of continously high ground-water level have cholera all the year round. Provinces of scanty rainfall have cholera in the rainy season and it disappears in the dry season. Both high temperature and high barometric pressure are favourable to cholera prevalence. Hardie, of Queensland, has found the same relation between pressure and typhoid as the author found in Bombay between cholera and pressure. The period of highest barometric pressure corresponds fairly with the period of highest mortality, the higher the barometer during any season of the year, the greater being the death-rate. "

Gordon, C. A. ([58]), states that atmospheric conditions during epidemics have been various, except with the general existence of an increased hygrometric state.

In Bengal, cholera is coincident with a seasonal deficiency of rain and is most prevalent from March to November. In Bengal, it is present during the earlier part of the year, towards the south-west of India during the later part, and in West India during June, July and August.

Gallas ([65]) remarks that, in 1910 and 1911, the curves of rainfall and external temperature varied fairly closely with the cholera incidence in French India. In October 1910, however, when the rains were very heavy, the epidemic stopped, while, in 1911, with moderate rains, the epidemic continued. He believes this to be due to the effective cleansing influence of very heavy rains, while moderate rains encourage the growth of the organisms outside the body. Causes of epidemics include, among others, diarrhœa due to sudden fall of temperature occasioned by rains.

In the Philippines ([66]), the relations of climatic factors to cholera incidence have been carefully studied. Charts showing barometric pressures, atmospheric temperatures and humidity are compared with those showing cholera incidence, and "while there are apparently some related factors to be seen, so far they are so elusive that nothing definite can yet be stated. It may be that there exist additional causative factors which must operate synchronously to produce a cholera outbreak. The only definite and constant causative factor so far discovered is the constant presence of cholera-carriers in the community."

King ([67]) writes of his cholera clock for the Madras Presidency and says: "Whilst both the north-east and south-west monsoons affected a district, its chief cholera season would follow its chief monsoon", and he recognised "meteorological influence as of importance solely in so far as it affected the distribution and vitality of the comma bacillus". "Later observations showed me that, if cholera were introduced into a district in other than the period following its chief monsoon, it would fizzle out."

Rainfall and Humidity.

In connection with rainfall, Bellow ([2]) writes: "The severer epidemics appear to have taken place during the seasons of drought and famine, and to have been aggravated during the first falls of rain, and, as rainfall increased and both soil and air became super-saturated, the disease has abated generally in strict relation with the nature of the rainfall, *e.g.*, in Assam, very clearly heavy rainfall following drought is usually attended with increased activity of cholera. In Burma also, the cycle and the cholera is certainly influenced in respect to the intensity of its prevalence by the effects of rainfall in respect chiefly to temperature and humidity. The North-West Provinces and Oudh show that cholera in its cycle is steadily and uniformly affected, *e.g.*, to its seasonal activity, by the character of the rainfall."

Pagliani ([68]) asserts that "the epidemic was reduced to only a few cases when a heavy rainfall occurred, and, in a few days, numerous cases of diarrhœa and some of true cholera were reported."

Clemow [59] also concludes that light rainfalls appear "to favour the spread of cholera".

Chantemesse [69] writes that "twice during October rain had fallen and each fall had been followed two to three days later by a smart recrudescence of the epidemic." Another two similar incidents produced the remark that "the rainfall had once more clearly indicated its close relationship with the propagation of the epidemic."

Banks [70], in his observations at Puri, notes that: (*a*) slight showers revivify the virus of the disease; (*b*) with moderate continued showers the germs rapidly propagate themselves; and (*c*) copious rainfall and abundant water dilutes the germs so much as to destroy their virulence and check the progress of the disease.

The same author, in another paper [71], says the disease prevailed chiefly through periods of scanty rainfall accompanied with a high temperature of the atmosphere.

Nothnagel [5] remarks: "A heavy rainfall in dry regions with porous soil may increase the predisposition to cholera, while the same in damp places, by putting an extensive surface under water and perhaps washing away the filth, may lessen it."

Stamm, Johannes [72] writes: "In certain areas in India subject to two monsoons, cholera is under favourable conditions in the greater monsoon. If cholera be introduced at any other period, it can be readily suppressed. But an epidemic does not get a real hold of an area until about six weeks after the breaking of the monsoon. The subsoil water begins ordinarily to undergo a marked rise about this period of the monsoon."

Morrison and Fox [73] write that cholera outbreaks in Poona in 1914 were water-borne, and originated in cases occurring in the catchment area. No reliable evidence exists of a house-to-house infection, but a marked correlation was found between rainfall in the infected areas and the incidence of cholera in Poona.

Highet [74] describes cholera in Bangkok, which stands on a river 25 miles from the bar. "Cholera is very prevalent, commencing late in December and continuing till April, thus prevailing during the dry season of the year. If heavy rains fall about the end of April and early in May, the river rises and the increased flow soon stops the disease. The lower the level of the river, the more sea-water enters, and the greater is the accumulation and so concentration of the sewage."

Flu, C. [61], concludes that: (*a*) dry seasons favour epidemic outbursts of cholera, while during the rainy seasons only sporadic cases occur; and (*b*) rain acts in many ways against a spread of the disease. A single shower, on the other hand, may increase the risks of infection.

The United States Commission Report on Cholera ([55]) states that in Sylhet, Assam, it has been noticed that, as soon as the country becomes dry, cholera makes its appearance and remains till the inundations set in. With the dry season come reports of cholera from every direction, almost simultaneously and springing up like a plant of the season. As soon as the rains have set in, cholera as a rule disappears or all but disappears.

Soil and Subsoil Water.

Pettenkefer ([75]) entertains the belief that cholera never prevails epidemically on rock, and accounts for this supposed fact on the principle that excrement cannot penetrate into the soil and that rock neither absorbs nor gives off moisture.

Bellew ([2]), talking of endemic foci of cholera, says:

> "The main features of the physical geography of these places are a low-lying alluvial soil, more or less supersaturated with ground-water in a state of stagnation, or with very slight motion, and subject to periodical inundations or waterlogging by the seasonal floodings of the great rivers by which the areas in the deltas are traversed. In the epidemic regions of cholera, every sort of physical aspect is met with, but collateral circumstances favourable to the continued prevalence of cholera include certain conditions of soil favouring sudden and unduly active evaporation of moisture from its surface, as in normally arid areas when rain moistens the parched surface, and as in normally waterlogged or submerged areas when the excess of water is drained away and the soil begins to dry, and as, in both cases, when seasons of unusual drought are followed by copious rainfall or are attended by periods of humidity of the atmosphere without rainfall but with unusually high temperature."
>
> "There are certain districts in Madras Presidency, which, in their conditions of soil and climate, approach very nearly to the conditions of soil and climate which characterise the area of Lower Bengal, the acknowledged natural *habitat* of cholera. The delta of the Cauvery is proved to be a favourite haunt of cholera, and the delta of the Godaveri, in respect to conditions of soil and subsoil moisture, is almost identical with that of the Cauvery delta. When the soil of India is drained as well as that of England, then, and not till then, may we hope for any sensible diminution in the prevalence of cholera."

Emmerich and Jusbaschian ([76]) say that virulent cholera is caused only by organisms which have come from the soil, and only from soil which has been dry for lengthy periods, during which a gradual accumulation of suitable food has been collected in the ground by capillary upflow from the deeper layers.

Cheilewizky ([77]) concludes that mere contamination of soil with manure and similar material is not enough to produce conditions favourable to the growth of

cholera, a long dry period being required to allow of the transference of suitable nutriment in adequate quantity to the surface layers.

Stamm, Johannes (72), in his work regarding non-agglutinable cholera-like vibrios in water, says: "It is possible to revive a theory that the vibrio in subsoil water is a debilitated true cholera vibrio capable of change of vigour as a result of the water becoming charged with various salts from the subsoil." He has come to the conclusion that "the period in which marked mortality from cholera occurs is that immediately following the greatest fall of the subsoil water and heralds a commencing rise".

Flu, C. (61), states that no specific influence can be said to be exerted by either soil or water. Earth, even when locally and temporarily "disposed" to cholera, does not play the specific role in a cholera epidemic that Pettenkofer assigned to it.

King (78) expresses the opinion that, "as a rough average, water under monsoon influences, acting upon a soil that has been dried by a preceding hot season, takes about six weeks to effect permeation sufficient to add largely to the subsoil water table. During this interval, fresh salts of sorts, plus dilution by a comparatively microbe-free and soil-filtered clean water, have been added to the concentrated and microbe-crowded waters of the dry season. The cholera vibrio is thus placed under favourable circumstances at certain seasons or attainment of virulence, becoming temporarily the predominant microbe, both in a typical form in wells and in the intestine of man. Such hypotheses would fit in fairly well with Pettenkofer's theory regarding Munich.

Temperature and Pressure.

Herbert (16) says that both high temperature and high barometric pressure are favourable to cholera.

Banks (70), writing from Puri, says that the temperature of the atmosphere is of subordinate importance in the causation of epidemics of cholera."

Nothnagel (5) adds: "So striking a dependence on external temperature, as epidemics reach their maximum in August and September, shows unmistakably that the bacillus requires for its growth and development certain conditions, not only in the external world but also in the human body".

Bruce Low (47) writes that "certain conditions, including high temperature, are believed to favour the development of cholera outbreaks".

Simond (79) remarks that "a marked lowering of the temperature was on several occasions associated with the cessation of an epidemic, but whether this acted directly

on the organism outside the body or indirectly through its effect on the carriage of infection by flies was not determined ".

Greig ([32]) writes: "Temperature has a most important bearing on the extra-corporeal life of the cholera bacillus. During the colder months in Calcutta, the life of the vibrio was longer than during the hot months, consequently the critical months in Calcutta as regards cholera are the colder months. These critical months immediately precede, it is to be noted, the annual recrudescence of cholera in Calcutta, which takes place in the months of February, March and April. "

Tull Walsh ([80]), in his general review of cholera, says: "Temperature forms an important item in shortening the extra-corporeal life of the cholera vibrio. In Calcutta, the cold-season life is longer than the life during the hot and rainy months. The months in which an epidemic is most to be feared are the cold winter months (in India, at any rate), since, with lengthened extra-corporeal and saprophytic life, there is, when vibrios are expelled by 'carriers', a greater possibility of water and food infection."

India has for many years been recognised to be one of the most important endemic centres for cholera, and the sanitary reports of the Provincial and Imperial Governments have, year after year, proved that the losses by cholera among the Indian populations have been enormous. Because of its importance as a source of spread to other countries of the world, it has been the custom, in discussing the epidemiology of cholera, to ignore the epidemics in India as of relatively lesser importance, and to devote most time and energy to the task of tracing the methods and routes of spread of the disease from what has been so often called " the home of cholera ". Even in these days of quick travel and rapid international communications, this seems, however, to be a very short-sighted view, and in any case, for India itself, it is the initial local outburst or individual epidemic which is of primary importance.

If the causal factors of these periodic outbursts in India could be elucidated, then steps could be taken to combat them in the "home " of the disease, and the spread of cholera to other countries would automatically cease to be of any importance, provided, of course, that other "homes " of endemic foci did not exist. We have only to recall the immense losses suffered by most of the civilised and uncivilised nations of the world through the invasion of the disease to appreciate the great practical value which the solution of these questions might have.

It was from this point of view that it seemed worth while to make a detailed examination of an area suited to that purpose. It is probably correct to say that cholera is present in one or other part of the Madras Presidency throughout the twelve months of the year, and it has been already shown that certain parts of the Presidency are real endemic centres of the disease. The Presidency has, moreover, a population of nearly 43 millions, so it may be said to constitute a fairly good random sample of the 350 millions of the people of India. It would appear, therefore, that we have here an entirely suitable area for investigation, and the cholera figures used are the monthly mortality statistics for the period 1902-21.

Geographically, the Presidency of Madras may be roughly divided into two zones, the course of the Eastern Ghauts being the boundary line between the two areas. The northern zone receives the south-west monsoon, which falls during June to August, whilst the southern zone receives practically all its rainfall during the months of October to December from the north-east monsoon, which passes down the Coromandel coast. In the eastern centre of the Presidency, however, there lies a group of five districts which are fortunate enough to be affected to some degree by both monsoons, and for purposes of investigation, therefore, the figures for these three areas were considered separately, those of the northern area being classed as Group 1, the southern area as Group 2, and the central as Group 3.

In the first place, graphs were prepared showing monthly mortality figures for cholera and monthly rainfall over the twenty-year period. In Group 1, the graph showed that, while cholera is practically non-existent during the early months of the year, great and sudden exacerbations of the disease coincide with the onset of the north-west monsoon, the normal line being again reached about the commencement of the cold weather. As regards Group 2, while the north-east monsoon falls in October to December, cholera does not flare up as it does in Group 1, but reaches its maximum, which may be very high, only about six weeks to two months after the onset of the rains, and then gradually falls to a minimum at the beginning of the hot-weather months. In both groups, however, there is a single curve for the twelve-month period, *i.e.*, an annual periodicity coinciding to a greater or less extent with the monsoon period. In Group 3, which experiences both monsoons, the twelve monthly cholera incidence curve shows two maximal points, these corresponding roughly with the two periods of rainfall. It would appear, therefore, that in Madras Presidency some relationship exists between the incidence of cholera and the prevalence of rainfall, and the indications were that more exact methods of examination would throw further light on this point.

This was carried out by setting up correlation tables for monthly cholera deaths and rainfall for each group. It was necessary, in the first place, to take a monthly "moving average" for the cholera deaths over the 21-year period for each group, so that monthly deviation figures above and below the mean could be obtained. As in Group 2, the maximum incidence of the disease was not reached until a period of from six weeks to two months after the monsoon had commenced; in order to demonstrate this "lag" mathematically, the monthly rainfall figures were successively correlated: (*a*) not only with the cholera deviation figures for the same month, but (*b*) with those of the following month, (*c*) with those two months later, and (*d*) with those three months later. For example, June rainfall was correlated with the June cholera deviations and successively with the July, August and September deviations, and correlation coefficients for each were obtained. In Group 1, the maximum correlation occurred immediately the monsoon burst. The figure was $+.378 \pm .0377$, a very significant correlation coefficient, and one which proves that in this area a very close relationship exists between cholera and rainfall. In Group 2, the maximum correlation coefficient was only reached two months after the monsoon broke, but at this

period the highly significant figure of $+.477 \pm .0398$ was obtained. For Group 3, the two months' "lag" was also evident, at that period the correlation coefficient reaching a maximum of $+.338 \pm .0390$. It was obvious that, although the districts of Group 3 were affected by both monsoons, yet it was only during the north-east monsoon that cholera worked real havoc and that the same influences were at work as in those districts included in Group 2.

For all three areas, however, the rainfall is proved to have a very considerable and direct influence on the incidence of cholera, so much so, that it is often possible to predict accurately when cholera will make its appearance. It is not so easy to explain why the "lag" of two months should occur only in two of the three areas. The area comprised in Group 1 is very sparsely populated, whilst most parts of Groups 2 and 3 are fertile and are densely populated, so that density of population cannot be given as an explanation. It may be that the causal factor exists in the very nature of the rainfall itself. The districts in Group 1 have a very meagre rainfall, with long periods of drought — existing, in fact, more or less constantly in danger of famine; and the first showers of the monsoon fall on a dry and cracked black-cotton soil and doubtless wash the large accumulations of surface filth from the hard-baked ground into every drinking-water well and tank.

An examination of the cholera and rainfall statistics for Bombay Presidency, which derives its rain wholly from the south-west monsoon, reveals the fact that there also a yearly periodicity of cholera occurs, the maximum incidence coinciding with the rainy season. In Bengal, however, this apparently does not hold good, although lack of time has forbidden any mathematical treatment of the figures.

The natural sequel to the above investigations was an examination of the relationship, if any, between cholera and other meteorological factors. The figures for humidity were correlated with the cholera deviation figures exactly as was done in the case of rainfall; but, somewhat surprisingly, every correlation coefficient obtained was either negative or was insignificant compared with its probable error for all three groups of districts, either with or without a period of "lag". It seems, therefore, that humidity of the atmosphere by itself plays little or no part as a factor affecting the incidence of cholera in Madras Presidency, in spite of the statements to this effect made by numerous writers on the subject.

It has not been so far found possible to obtain reliable figures for temperature or atmospheric pressure, so that the theory that these factors influence the incidence of cholera has not been tested mathematically. Generally speaking, and especially in view of our present knowledge regarding the important part played by carriers, one would have inferred that factors such as pressure of the air and depth and movement of subsoil water could exert very little influence.

The fact remains, however, that in Southern India, at least, the seasonal periodicity in the incidence of cholera is very intimately related with the monsoons. With the fall of rain great changes in humidity of the atmosphere and in temperature doubtless take place, and the question arises as to the influence, if any, these changes exert upon the comma bacillus, whether it be present in the intestines of the human carrier

or living in the outside world. Mathematically, it would appear that little if any effect is produced, but that is by no means the final word in the matter. Does the vibrio pass through a life-cycle, as has been suggested by Heiser ? Does the increase in humidity and the fall in temperature give rise to conditions favourable to the propagation and increased virulence of the bacillus ? Does the immunity of the population fall as a result of chill or from other causes ? These are all questions of supreme importance, which it is not easy to answer, but the reply to which might throw immense light on the epidemiological problems connected with the disease.

McKendrick would have it that no reply is at present possible, as our experience is very curtailed owing to the fact that the vast majority of the smaller epidemics are never reported, and that our general experience is based only upon those larger epidemics which demand recognition. Our experience, he says, ([108]) is not an experience of the usual but an experience of aberrant types, which are of comparatively rare occurrence. "To use an analogy, our experience is similar to that which we should gain regarding speculation if we had to depend upon reports received from those who had made fortunes." There is no doubt that, in the case of cholera, in endemic centres such as India, official statistics seldom or never include the smaller epidemics. At the same time, cholera is an easily recognised disease, and is one with which the Indian people are only too well acquainted, so that if the available figures are taken over a period of years they give a fairly accurate representation of the incidence of the disease. That being so, and giving due weight to all that McKendrick has to say regarding the causes of the rise and fall of epidemics, it may be held that there still remains justification for the assumption that some light has been thrown on the problems connected with cholera, and the above investigation has demonstrated at least one important fact and has indicated one of the lines on which further work on the epidemiology of the disease must be carried out.

SEASONAL PREVALENCE.

There can be no difference of opinion regarding the seasonal prevalence of "periodicity" of cholera. This feature of the disease has been recognised wherever cholera has been experienced.

Bellew ([2]) writes that "in the annual alternations of rise and fall in cholera prevalence it is observed, as a regularly recurring phenomenon of the disease, that the periods of the vernal and autumnal equinoxes are the season of its absolute inactivity, or minimum degree of prevalence, even in the course of an epidemic; and that the months intervening between these and the northern or summer and the southern or winter solstices respectively are the seasons of its habitual activity or maximum degree of continuity. This regularity is real and fixed both for endemic, or tropical, and for epidemic, or non-tropical, areas of cholera prevalence."

Pettenkofer's ([97]) remarks on the same subject are of much interest. He quotes figures of the disease in the Kingdom of Prussia from the year 1848 to 1860, during which period cases of cholera occurred every year, and shows how the great majority of the deaths took place during the months of August, September and October. "In the face of such a fact, which is independent of any theoretical consideration — in the face of this astounding regularity in the rise and fall in number of cases according to months — one may well feel constrained to take the seasonal element into account, and to assume the dependence of cholera and the infecting cholera fungus on a seasonal element as well as on locality."

Macpherson ([3]) says that the seasons of cholera have been tolerably well ascertained in Bengal. In the lower provinces the great season is the hot weather, and there is almost always a large diffusion of disease at this period. In the early part of the cool weather the disease appears to have a new period of increase. As we pass to the north-west, the period for epidemics appears to be retarded, and it occurs after the setting-in of the rains. In the Punjab, it appears still later in the year. In the North-West Provinces the disease is almost extinct in the cold weather, which is by no means the case in Lower Bengal.

A. Hirsch ([81]) shows, from an examination of 920 epidemics outside India, the dependence of cholera on the season.

Dr. Paul Clements ([35]) says: "The incidence curve (of cholera) is so typical that the writer has often predicted accurately the termination of an outbreak in a given locality with the same confidence as the physician predicts the return of the temperature to normal in a case of pneumonia."

Nothnagel ([5]), in reviewing the controversy between Koch and Pettenkofer, says that "there must be added to the bacillus a predisposition brought about by season or place or locality. The striking dependence of the bacillus on external temperature shows that the germ requires for its growth and development certain conditions not only in the external world but also in the human body".

PERIODICITY OF CHOLERA EPIDEMICS.

During recent years the question of "periodicity" has been largely discussed in connection with a number of infectious diseases, such as measles, influenza and malaria. That this phenomenon is no new feature of cholera epidemics is evidenced by the fact that Bellew ([2]), in 1884, drew attention to it, and produced statistics from every province in India to show that there is not only an annual periodicity in the incidence of the disease but that a triennial periodicity of recurring cholera epidemics also occurs. Using figures for the period from 1862-81, he tries to show that cholera

tends to run a definite course of revival, decline and subsidence in the successive years of each triennial cycle, although these occur with varying degrees of intensity not only in the different years but in their component years as well. This successive course in the cyclical prevalence of the disease, he states, is clearly shown in the mortality returns for each district.

Gordon, C. A. (58), discussing cholera in India from 1842-79, states that "sometimes no epidemic follows sporadic cases. Sometimes a sudden outbreak occurs, in other instances it appears gradually. In some cases it has quickly culminated and disappeared, in others more slowly, and the infection has persisted during longer periods. The occurrence of epidemics is periodic, the apparent conditions of particular localities affected remaining unaltered meanwhile. The duration of intervals between such epidemics extends on certain occasions to several years."

Nothnagel (5) thinks that the cholera bacilli go through a stage of evolution outside the body before they can cause the disease, and adds that Von Pettenkofer is correct when he says that the presence of bacilli is not all that is necessary to cause an epidemic, but a series of local conditions are required as well. What these are Von Pettenkofer and his school have not told us, he adds, but it is obvious that, although Nothnägel does not mention the word periodicity, he had that in mind.

Clemow (59) concludes that "a district which in the first year of an epidemic suffers severely may be expected to escape lightly in the second year, and to a certain extent the reverse holds good".

Clemow (60) again alludes to periodicity when he writes of the arrival in Camaran of several ships from Bombay in the summer of 1912. He says: "This raises the question whether the cholera virus in its endemic home is not once more taking on that unknown quality which from time to time seems to give to the disease the power to extend widely outside the endemic area."

In 1914, he writes that the disease "was only sporadic in Turkey and the Dardanelles, and did not take on the characters of a disastrous epidemic". This would seem to confirm the view put forward before that the cholera prevalence in this part of the world during the past two years and more has been due to a relatively non-malignant and inactive virus, that the virus has acquired these qualities during the many years that have elapsed since it reached Europe from its epidemic home in India, and that, if this prevalence had been brought about by a fresh importation from India, there would have been a very different tale to tell."

He seems, however, to have forgotten that there actually was a fresh importation from India to Camaran in the summer of 1912. He makes no attempt to explain why this did not spread widely in malignant fashion. The fact that no such widespread re-infection took place would surely confirm a periodicity of the disease. As British delegate on the International Board of Health at Constantiople in 1914, he again

states that "the present cholera virus in Europe is one which appears to have lost to a great extent its virulence and primitive force, owing, no doubt, to the long period that has elapsed since its introduction to Europe from the endemic home of cholera in India."

Simpson ([21]) confirms this point of view by stating that "Mecca has been the one important gateway through which cholera has entered Europe, though there were often others simultaneously. There is, however, much variancy in the virulence of epidemics of cholera."

Flu, C. ([61]), also concludes that great periodicity is observed in the epidemic outbursts of cholera, and this periodicity stands in relationship to the immunisation which each outbreak of cholera effects in the population, an immunisation lasting apparently six months. He is obviously here thinking of the annual periodicity so regularly noticed in India.

The United States Commission on Cholera ([55]) makes more than one reference to "the very obvious periodicity of cholera epidemics in India", and also gives statistics to prove the occurrence of a seasonal prevalence of the disease. In the same connection, the report quotes Koch as writing, in 1885, that "the periodical behaviour of cholera is up to the present far too little appreciated. It has the most important influence upon the course of cholera in India and by reference to it certain peculiarities of cholera in India may be easily explained." "The periodicity of cholera warrants the inference that there is an immunity following recovery from the disease, and cholera is therefore in the same class in this respect with the genuine infectious diseases." "An extensive invasion of the population of India leaves behind it an immunity of about three to four years' duration, after which time always a new epidemic, wave-like, again spreads out from its endemic resting-place, pursuing the main highways of commerce towards the north-west of India. Bryden first thoroughly studied these three to four-year periods of the curves of cholera prevalence, and sought to indicate them graphically. He did not, however, discover the correct explanation of these appearances, but he thought they owed their origin to the monsoon."

Koch explains the periodicity "mainly through the influence of the immunity which follows extensive ravages of the disease. He also thinks that, to acquire immunity, it is not necessary to suffer the disease in its severest form, but that even a slight illness gives protection, and that, by slight, hardly noticeable attacks, a far greater portion of the inhabitants will be looked on as having been infected than one would infer from the number of cholera cases announced or from the mortality records. Within the endemic area of Bengal the periodicity of cholera is but little marked. Outside of the endemic area, where cholera has raged one year, there is almost invariably a period of marked freedom from epidemics varying from three to five years."

As long ago as 1895, Colonel King, I.M.S., pointed out the annual or seasonal periodicity of cholera incidence in Madras Presidency, and when the whole area was divided into the three groups of districts, affected in varying fashion by the two monsoons, and separate graphs of the monthly cholera deaths in each of these groups were prepared, it was evident that King was correct when he wrote, "if cholera were introduced into a district in other than the period following its chief monsoon, it would fizzle out". The graphs show that this is exactly what did happen for the period of years under investigation, a period much later than that with which King was dealing. Not often does one find such corroborative independent evidence in the field of epidemiological research.

The graphs, however, not only showed the annual periodic curve but seemed to indicate that a much longer periodicity wave also came into play. The monthly mortality figures were therefore submitted to the method of periodogram analysis, a method adopted by Brownlee ([107]) in demonstrating periodicity in epidemics of measles and other infectious diseases. The results obtained were plotted in graph form, the units of the abscissa line representing months and those of the axis amplitudes. The annual periodicities were apparent at the 12-, 24-, 36-, etc., month periods but by far the highest amplitude was reached at the 72-month period, in each of the graphs for the three groups. As the maximum amplitude of the annual periodicity curve in Group 1 occurs at a different season of the year from that in Groups 2 and 3, and nevertheless the long periodic wave is exactly the same length in all three groups of districts, it is evident that cholera in Madras Presidency, over the period of years under examination, has gone through a six-yearly cycle.

Bellew, in attempting to prove that cholera passes through a triennial cycle in every province in India, was compelled to admit that various anomalies and irregularities as to time and severity occurred. These, he assumed, were easily to be understood in consideration of latitude, geographical position, season, life conditions, etc. Bellew, however, made no use of mathematical methods, but drew his conclusions from mere examination of tabular statements of the statistics; and, while it is interesting to note that the question of periodicity had attracted attention, nevertheless, it is not possible to believe that his triennial periodicity existed in fact.

Opportunity has not yet presented itself for a similar examination of the cholera statistics of other parts of India for the same and for other periods of years; but the 72-month wave is so methematically exact for each separate part of the Madras Presidency that one may reasonably expect a similar finding for the Bombay Presidency — at least, where it is known that the annual periodic incidence closely resembles that for Southern India. It may also well be that, although in Bengal the maximum incidence does not coincide with the monsoon period, the 72-month cycle may be found; and investigation on the same lines in the other endemic foci, such as Southern Russia or the Dutch East Indies, might throw still more light on this question. In any case, the facts presented indicate a valuable line for further research, where figures are available. If such a periodic wave should be found in other endemic

centres of cholera, it must very considerably help to lighten the task of those who take up future preventive work.

FOOD SUPPLY AND THE VITALITY OF THE POPULATION.

Bellew (2) insists that the character of the epidemics is determined mainly by the conditions of the food supply, being virulent and prolonged in duration in proportion to the intensity of famine and endurance of food scarcity. Certain conditions of the people, lowered health, less food and undue privations are all favourable to the prevalence of the disease.

Turner shows that epidemics in the City of Bombay are always most severe after periods of drought and famine in the surrounding districts owing to the influx of starving and destitute persons.

It has also been noted by Henri Poitevin (27) that "carriers" were much more common in a group of poor and destitute pilgrims than in those of another group much better off.

Heiser (83) gives the weak and unresistant physical condition of the people in the Philippines as one of the factors favourable to cholera spread.

It may be taken as certain that lowered vitality in a population, from whatever cause, will give the cholera bacillus a favourable soil for propagation; and where famine or scarcity prevails, we have "suitable conditions" for outbursts of the disease, whether it be a tropical or extra-tropical area. The history of Russia during recent years is an apt illustration of this fact.

CONCLUSION.

In bringing this review to a close, it must be admitted that many problems in connection with the disease remain unsolved, and it is not remarkable that Bertavelly (87) recently came to the conclusion that "we really know comparatively little of the epidemiology of cholera". After a personal experience of the disease over a period of years, and with the knowledge gained by a thorough search through the literature on the subject, one is constrained to admit that there is much truth in the remark. It is unfortunately too often the custom blindly to transfer a statement made by one author into succeeding volumes or papers on the same subject, and careful scrutiny frequently reveals the original opinion to have been based on very doubtful evidence. Every attempt has been made here to avoid such an error, and for this reason large numbers of papers have been rejected as valueless and do not appear in the attached bibliography.

SUMMARY.

1. Cholera has existed in India for many centuries in much the same form as it exists at present.

2. The area of Lower Bengal and the Gangetic valley is not the one and only endemic centre for cholera in India. The disease is very generally endemic in some degree throughout the greater part of the whole peninsula.

3. Other endemic centres are to be found in Central Asia, in the Shat-el-Arab area, in certain parts of the Federated Malay States, in Java and the Dutch East Indies, in Indo-China, in the Philippines, and probably in Southern China.

4. The "latent" infection in the human "carrier", who is always present in endemic areas, only requires "suitable conditions" in order to produce a fresh outburst of the disease.

5. A series of ten pandemics have been experienced since 1817, but the intervals between these invasions do not reveal any regular periodicity.

6. Mecca plays an all-important part in the spread of cholera through Western Asia, Northern Africa and Europe.

7. In six of the ten pandemics, cholera has followed the land route through Afghanistan or Persia and thence through the Caucasus and Transcaspia to Russia and Western Europe. In the other instances, the disease has been carried via the Red Sea more or less directly to Egypt and thence to the whole basin of the Mediterranean.

8. The spread of cholera is greatly facilitated by the gathering of travellers at pilgrim centres, fairs and religious festivals.

9. The periodic outbursts of cholera in the countries of the Far East arise from the endemic foci known to exist in that area, and the infection need not necessarily be imported from India.

10. Many writers have attempted to demonstrate a relationship between the incidence of cholera and climatic factors, such as rainfall, humidity, temperature and pressure.

11. In Madras Presidency, the correlation between cholera and rainfall is highly significant, whilst the figures for humidity give either negative or insignificant correlation coefficients with cholera.

12. The seasonal prevalence of cholera is a recognised feature of the disease wherever it has been experienced.

13. The periodicity of cholera epidemics, which has been noted by various workers in different parts of the world, follows a definite 72-month cycle in Madras Presidency over the period 1902-21.

14. Famine or scarcity, with the resulting lowered vitality in the population, produces "suitable conditions" for epidemic outbursts of cholera.

15. Many problems in connection with the epidemiology of cholera still remain unsolved.

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